

1	ATGGCGCCAC	CACCAGCTAG	AGTACATCTA	GGTGCGTTCC	TGGCAGTGAC
	TACCGCGGTG	GTGGTCGATC	TCATGTAGAT	CCACGCAAGG	ACCGTCACTG
1	MetAlaProP	roProAlaAr	gValHisLeu	GlyAlaPheL	euAlaValTh
51	TCCGAATCCC	GGGAGCGCAG	CGAGTGGGAC	AGAGGCAGCC	GCGGCCACAC
	AGGCTTAGGG	CCCTCGCGTC	GCTCACCTG	TCTCCGTCGG	CGCCGGTGTG
	rProAsnPro	GlySerAlaA	laSerGlyTh	rGluAlaAla	AlaAlaThrPro
101	CCAGCAAAGT	GTGGGGCTCT	TCCGCGGGGA	GGATTGAACC	ACGAGGCGGG
	GGTCGTTTCA	CACCCCGAGA	AGGCGCCCCCT	CCTAACTTGG	TGCTCCGCCC
35	SerLysVa	lTrpGlySer	SerAlaGlyA	rgIleGluPr	oArgGlyGly
151	GGCCGAGGAG	CGCTCCCTAC	CTCCATGGGA	CAGCACGGAC	CCAGTGCCCCG
	CCGGCTCCTC	GCGAGGGATG	GAGGTACCCT	GTCGTGCCTG	GGTCACGGGC
	GlyArgGlyA	laLeuProTh	rSerMetGly	GlnHisGlyP	roSerAlaArg
201	GGCCCGGGCA	GGGCGCGCCC	CAGGACCCAG	GCCGGCGCGG	GAAGCCAGCC
	CCGGGCCCCGT	CCCGCGCGGG	GTCCTGGGTC	CGGCCGCGCC	CTTCGGTCGG
68	AlaArgAla	GlyArgAlaP	roGlyProAr	gProAlaArg	GluAlaSerP
251	CTCGGCTCCG	GGTCCACAAG	ACCTTCAAGT	TTGTCGTCGT	CGGGGTCCTG
	GAGCCGAGGC	CCAGGTGTTC	TGGAAGTTCA	AACAGCAGCA	GCCCCAGGAC
	roArgLeuAr	gValHisLys	ThrPheLysP	heValValVa	lGlyValLeu
301	CTGCAGGTCG	TACCTAGCTC	AGCTGCAACC	ATGATCAATC	AATTGGCACA
	GACGTCCAGC	ATGGATCGAG	TCGACGTTGG	TAGTTTGAAG	TACTAGTTAG
101	LeuGlnValV	alProSerSe	rAlaAlaThr	IleLysLeuH	isAspGlnSe
351	AATTGGCACA	CAGCAATGGG	AACATAGCCC	TTTGGGAGAG	TTGTGTCCAC
	TTAACCGTGT	GTCGTTACCC	TTGTATCGGG	AAACCCTCTC	AACACAGGTG
	rIleGlyThr	GlnGlnTrpG	luHisSerPr	oLeuGlyGlu	LeuCysProPro
401	CAGGATCTCA	TAGATCAGAA	CGTCCTGGAG	CCTGTAACCG	GTGCACAGAG
	GTCCTAGAGT	ATCTAGTCTT	GCAGGACCTC	GGACATTGGC	CACGTGTCTC
135	GlySerHi	sArgSerGlu	ArgProGlyA	laCysAsnAr	gCysThrGlu
451	GGTGTGGGTT	ACACCAATGC	TTCCAACAAT	TTGTTTGCTT	GCCTCCCATG
	CCACACCCAA	TGTGGTTACG	AAGGTTGTTA	AACAAACGAA	CGGAGGGTAC
	GlyValGlyT	yrThrAsnAl	aSerAsnAsn	LeuPheAlaC	ysLeuProCys
501	TACAGCTTGT	AAATCAGATG	AAGAAGAGAG	AAGTCCCTGC	ACCACGACCA
	ATGTGGAACA	TTTAGTCTAC	TTCTTCTCTC	TTCAGGGACG	TGGTGCTGGT
168	ThrAlaCys	LysSerAspG	luGluGluAr	gSerProCys	ThrThrThrA
551	GGAACACAGC	ATGTCAGTGC	AAACCAGGAA	CTTCCCGGAA	TGACAATTCT
	CCTTGTTGTCG	TACAGTCACG	TTTGGTCCTT	GAAAGGCCTT	ACTGTTAAGA
	rgAsnThrAl	aCysGlnCys	LysProGlyT	hrPheArgAs	nAspAsnSer
601	GCTGAGATGT	GCCGGAAGTG	CAGCACAGGG	TGCCCCAGAG	GGATGGTCAA
	CGACTCTACA	CGGCCTTCAC	GTCGTGTCCC	ACGGGGTCTC	CCTACCAGTT
201	AlaGluMetC	ysArgLysCy	sSerThrGly	CysProArgG	lyMetValLy
651	GGTCAAGGAT	TGTACGCCCT	GGAGTGACAT	CGAGTGTGTC	CACAAAGAAT
	CCAGTTCCTA	ACATGCGGGA	CCTCACTGTA	GCTCACACAG	GTGTTTCTTA
	sValLysAsp	CysThrProT	rpSerAspIl	eGluCysVal	HisLysGluSer

FIG. 1A

701	CAGGCAATGG	ACATAATATA	TGGGTGATTT	TGGTTGTGAC	TTTGGTTGTT
	GTCCGTTACC	TGTATTATAT	ACCCACTAAA	ACCAACACTG	AAACCAACAA
235	GlyAsnG1	yHisAsnIle	TrpValIleL	euValValTh	rLeuValVal
751	CCGTTGCTGT	TGGTGGCTGT	GCTGATTGTC	TGTTGTTGCA	TCGGCTCAGG
	GGCAACGACA	ACCACCGACA	CGACTAACAG	ACAACAACGT	AGCCGAGTCC
	ProLeuLeuL	euValAlaVa	lLeuIleVal	CysCysCysI	leGlySerGly
801	TTGTGGAGGG	GACCCCAAGT	GCATGGACAG	GGTGTGTTTC	TGGCGCTTGG
	AACACCTCCC	CTGGGGTTCA	CGTACCTGTC	CCAGACAAAG	ACCGCGAACC
268	CysGlyGly	AspProLysC	ysMetAspAr	gValCysPhe	TrpArgLeuG
851	GTCTCCTACG	AGGGCCTGGG	GCTGAGGACA	ATGCTCACAA	CGAGATTCTG
	CAGAGGATGC	TCCCGGACCC	CGACTCCTGT	TACGAGTGTT	GCTCTAAGAC
	lyLeuLeuAr	gGlyProGly	AlaGluAspA	snAlaHisAs	nGluIleLeu
901	AGCAACGCAG	ACTCGCTGTC	CACTTTCGTC	TCTGAGCAGC	AAATGGAAAG
	TCGTTGCGTC	TGAGCGACAG	GTGAAAGCAG	AGACTCGTCG	TTTACCTTTC
301	SerAsnAlaA	spSerLeuSe	rThrPheVal	SerGluGlnG	lnMetGluSe
951	CCAGGAGCCG	GCAGATTTGA	CAGGTGTCAC	TGTACAGTCC	CCAGGGGAGG
	GGTCCTCGGC	CGTCTAAACT	GTCCACATGT	ACATGTCAGG	GGTCCCCTCC
	rGlnGluPro	AlaAspLeuT	hrGlyValTh	rValGlnSer	ProGlyGluAla
1001	CACAGTGTCT	GCTGGGACCG	GCAGAAGCTG	AAGGGTCTCA	GAGGAGGAGG
	GTGTCACAGA	CGACCCTGGC	CGTCTTCGAC	TTCCAGAGT	CTCCTCCTCC
335	GlnCysLe	uLeuGlyPro	AlaGluAlaG	luGlySerG1	nArgArgArg
1051	CTGCTGGTTC	CAGCAAATGG	TGCTGACCCC	ACTGAGACTC	TGATGCTGTT
	GACGACCAAG	GTCGTTTACC	ACGACTGGGG	TGACTCTGAG	ACTACGACAA
	LeuLeuValP	roAlaAsnG1	yAlaAspPro	ThrGluThrL	euMetLeuPhe
1101	CTTTGACAAG	TTTGCAAACA	TCGTGCCCTT	TGACTCCTGG	GACCAGCTCA
	GAAACTGTTC	AAACGTTTGT	AGCACGGGAA	ACTGAGGACC	CTGGTCGAGT
368	PheAspLys	PheAlaAsnI	leValProPh	eAspSerTrp	AspGlnLeuM
1151	TGAGGCAGCT	GGACCTCACG	AAAAATGAGA	TCGATGTGGT	CAGAGCTGGT
	ACTCCGTCGA	CCTGGAGTGC	TTTTTACTCT	AGCTACACCA	GTCTCGACCA
	etArgGlnLe	uAspLeuThr	LysAsnGluI	leAspValVa	lArgAlaGly
1201	ACAGCAGGCC	CAGGGGATGC	CTTGTATGCA	ATGCTGATGA	AATGGGTCAA
	TGTCGTCCGG	GTCCCCTACG	GAACATACGT	TACGACTACT	TTACCCAGTT
401	ThrAlaGlyP	roGlyAspAl	aLeuTyrAla	MetLeuMetL	ysTrpValAs
1251	CAAACTGGA	CGGAACGCCT	CGATCCACAC	CCTGCTGGAT	GCCTTGAGGA
	GTTTTGACCT	GCCTTGCGGA	GCTAGGTGTG	GGACGACCTA	CGGAACCTCT
	nLysThrGly	ArgAsnAlaS	erIleHisTh	rLeuLeuAsp	AlaLeuGluArg
1301	GGATGGAAGA	GAGACATGCA	AAAGAGAAGA	TTCAGGACCT	CTTGGTGGAC
	CCTACCTTCT	CTCTGTACGT	TTTCTCTTCT	AAGTCCTGGA	GAACCACCTG
435	MetGluG1	uArgHisAla	LysGluLysI	leGlnAspLe	uLeuValAsp
1351	TCTGGAAAGT	TCATCTACTT	AGAAGATGGC	ACAGGCTCTG	CCGTGTCCTT
	AGACCTTTCA	AGTAGATGAA	TCTTCTACCG	TGTCCGAGAC	GGCACAGGAA
	SerGlyLysP	heIleTyrLe	uGluAspGly	ThrGlySerA	laValSerLeu
1401	GGAGTGA				
	CCTCACT				
468	GluOP*				

FIG._1B

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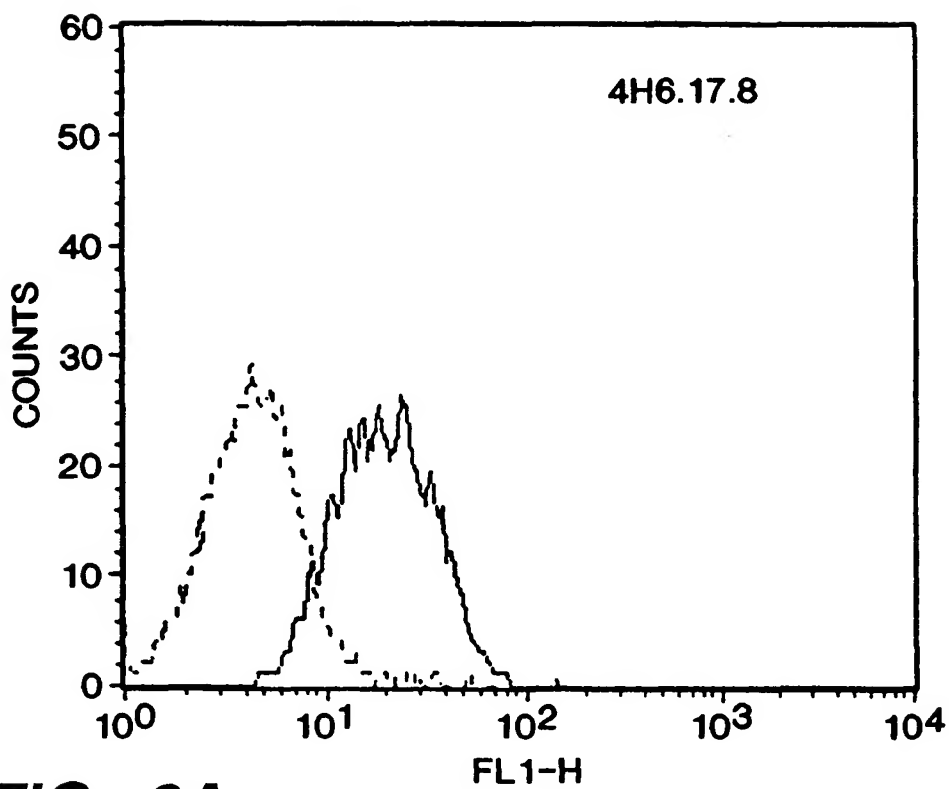


FIG. 2A

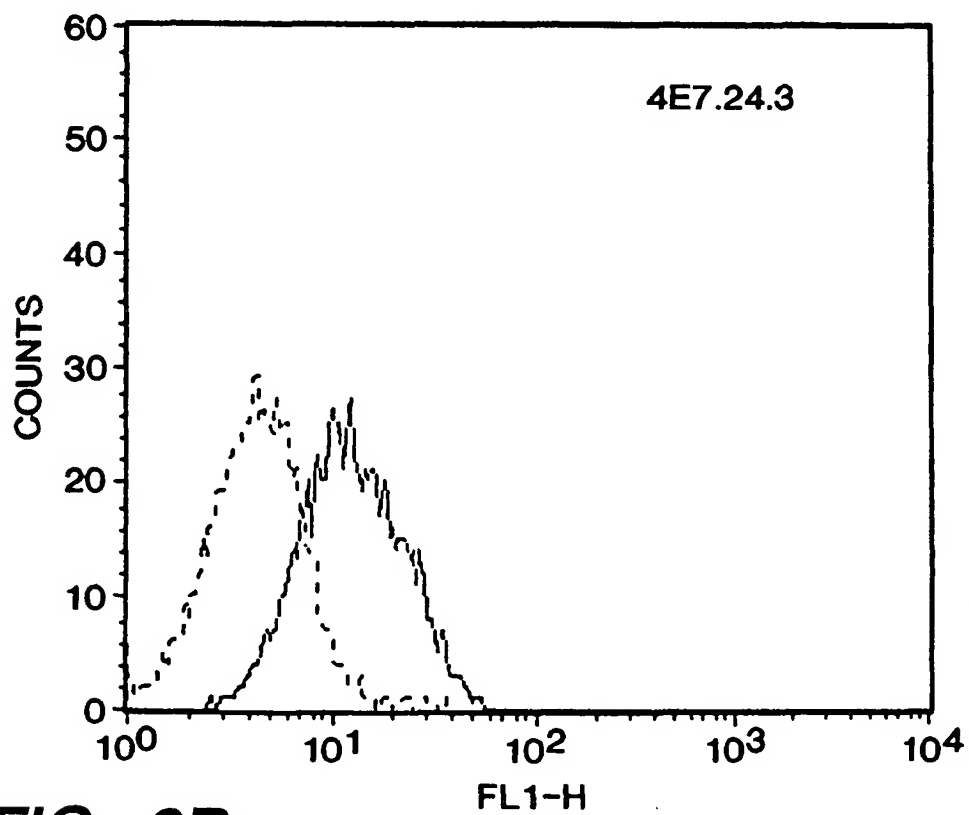


FIG. 2B

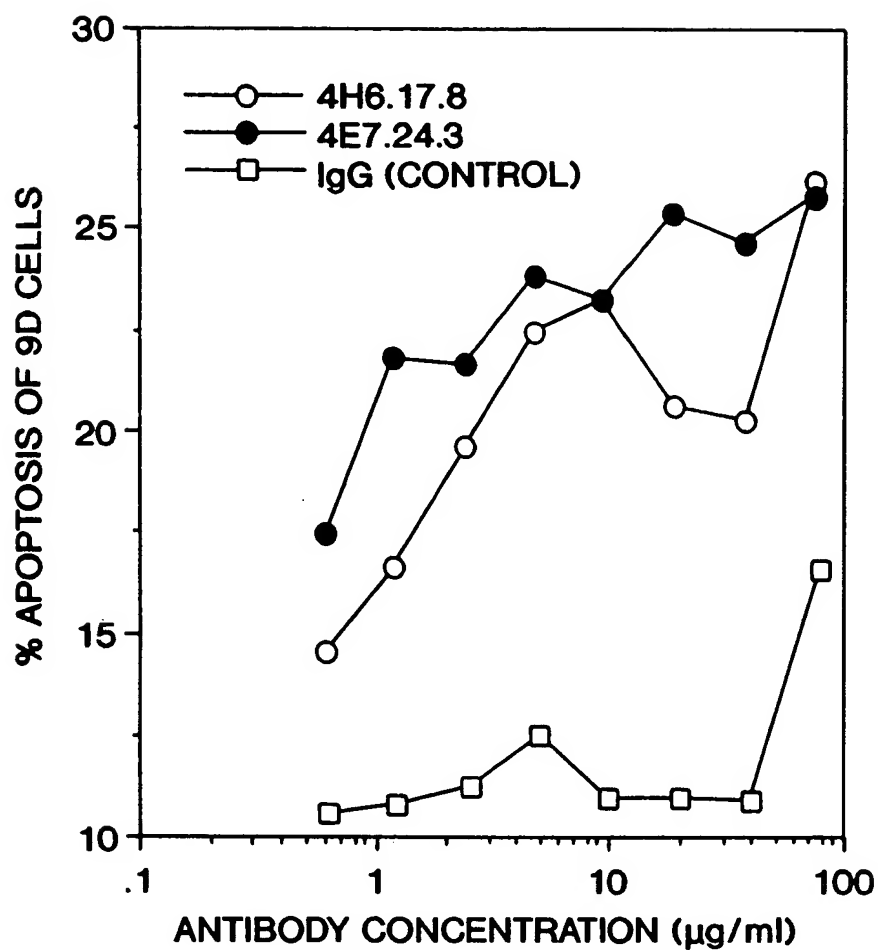


FIG._3

AFFINITIES OF Apo2Rs AND mAbs

		AFFINITY (pM)
DR4-IgG	to Apo2L	82
DR5-IgG	to Apo2L	1
mAb 4E7	to DR4-IgG	2
mAb 4H6	to DR4-IgG	5
mAb 5G11	to DR4-IgG	22
mAb 3F11	to DR5-IgG	20
mAb 3H3	to DR5-IgG	3

Affinities were determined using KinExA

FIG._7

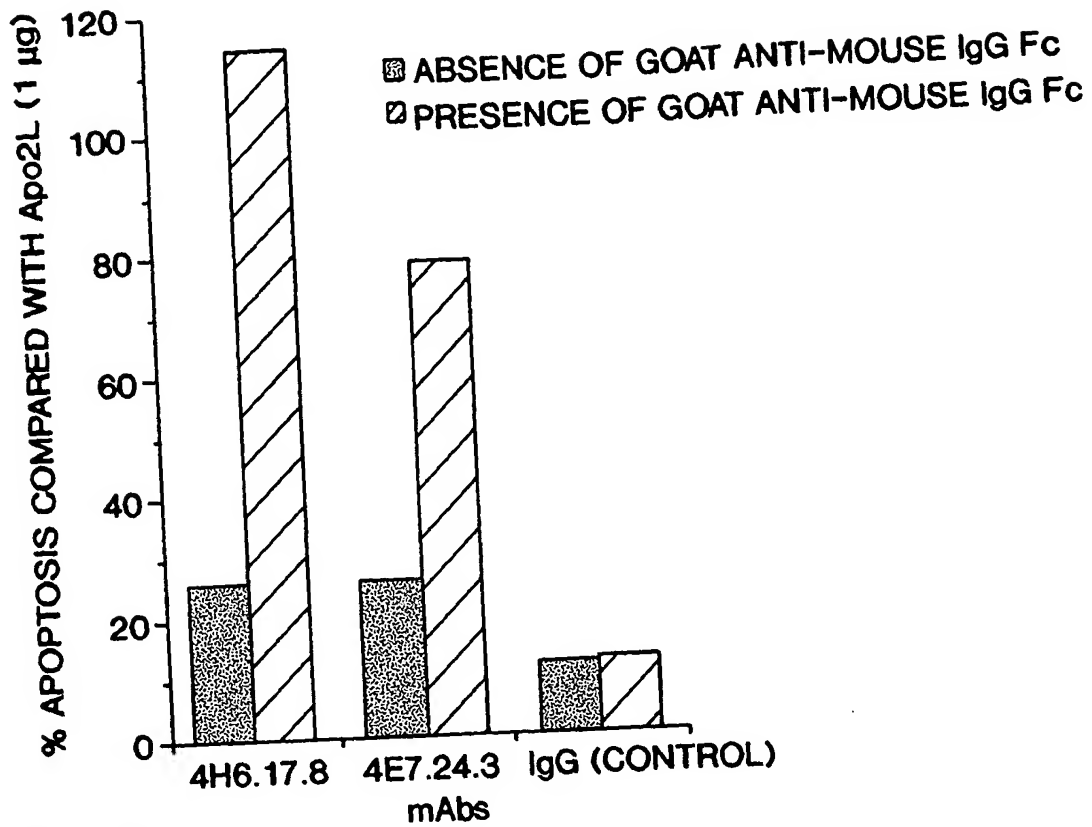


FIG. 4

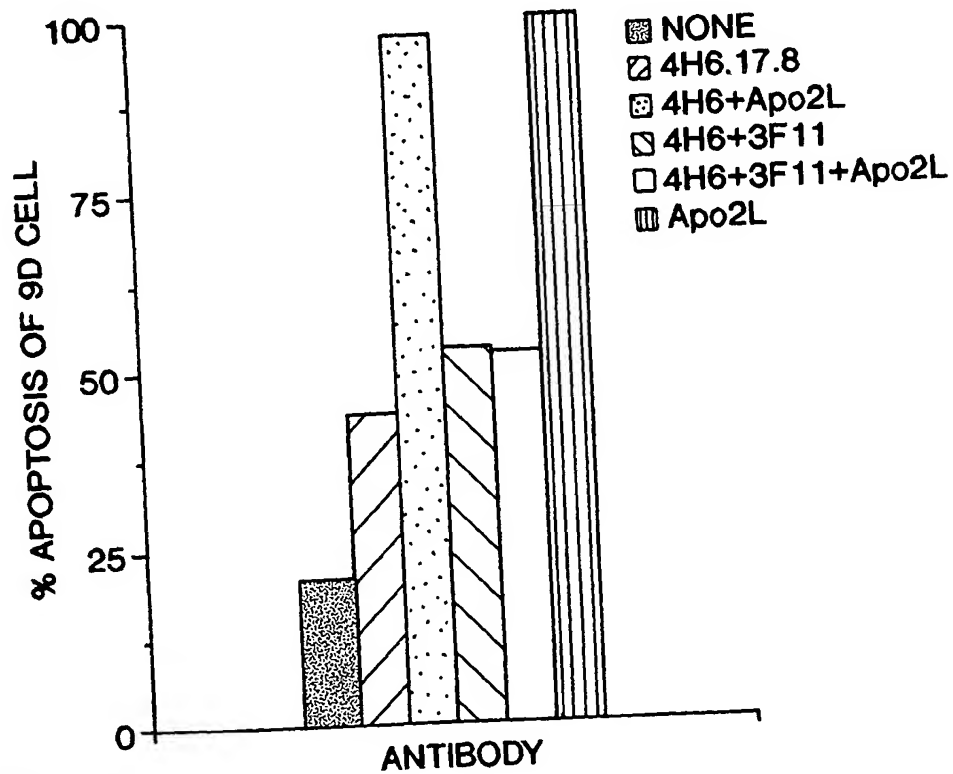


FIG. 5

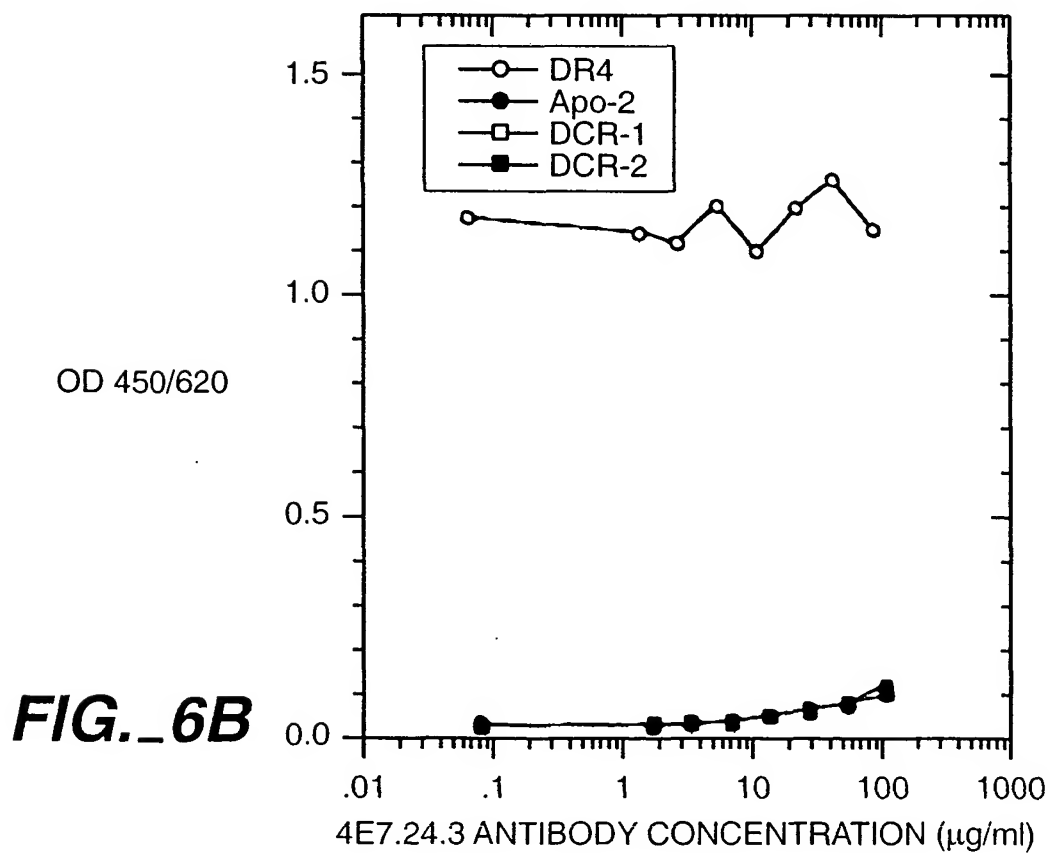
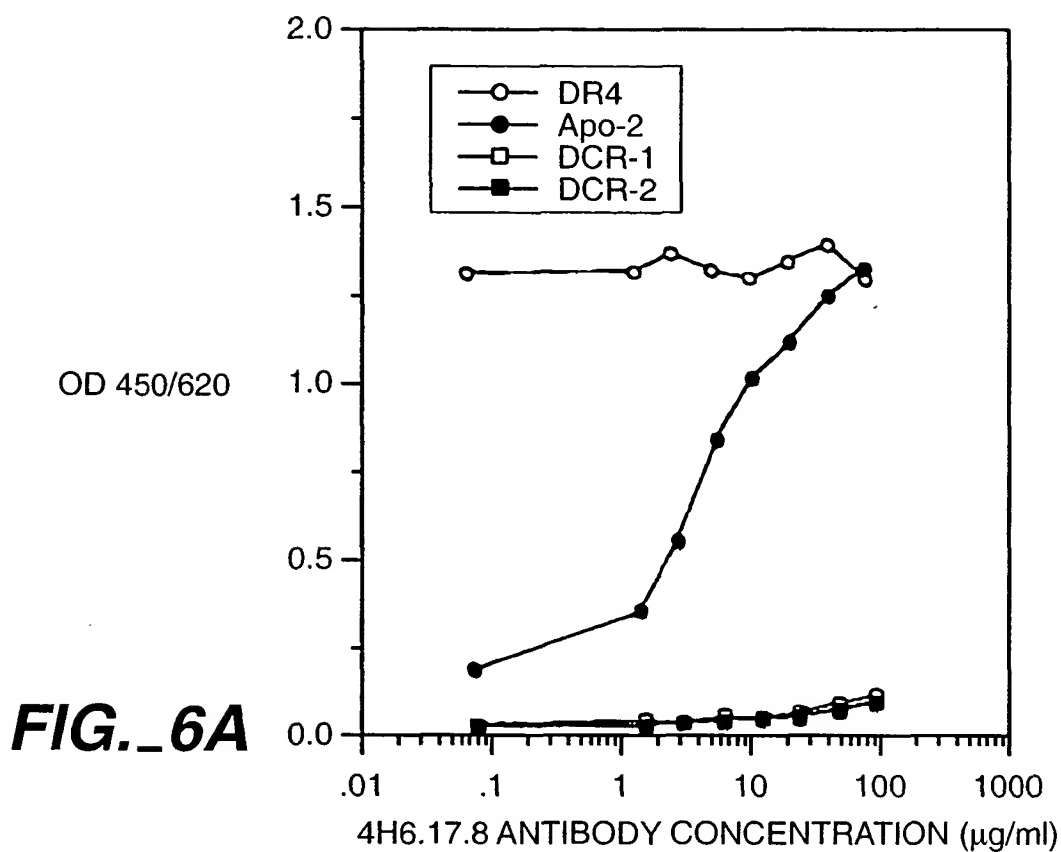
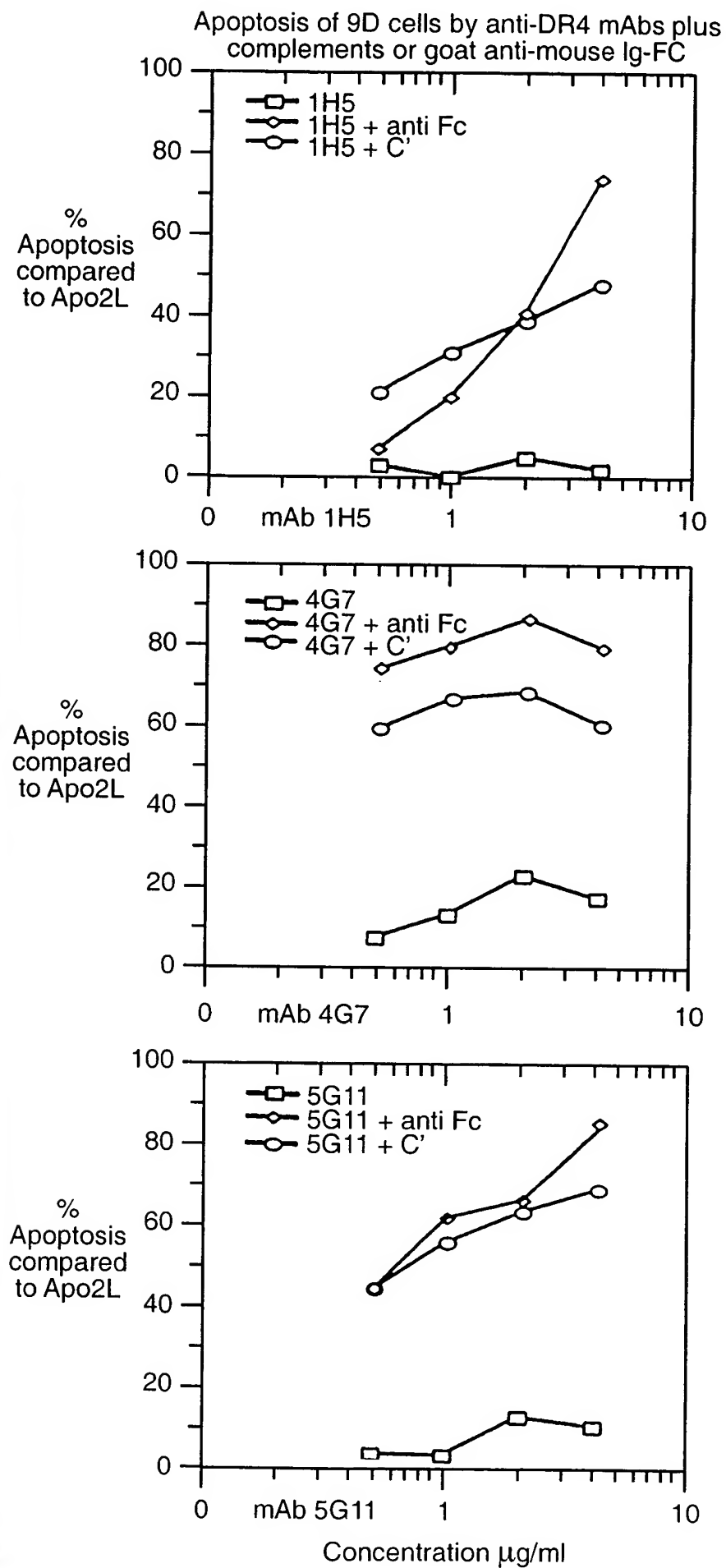


FIG. 8A



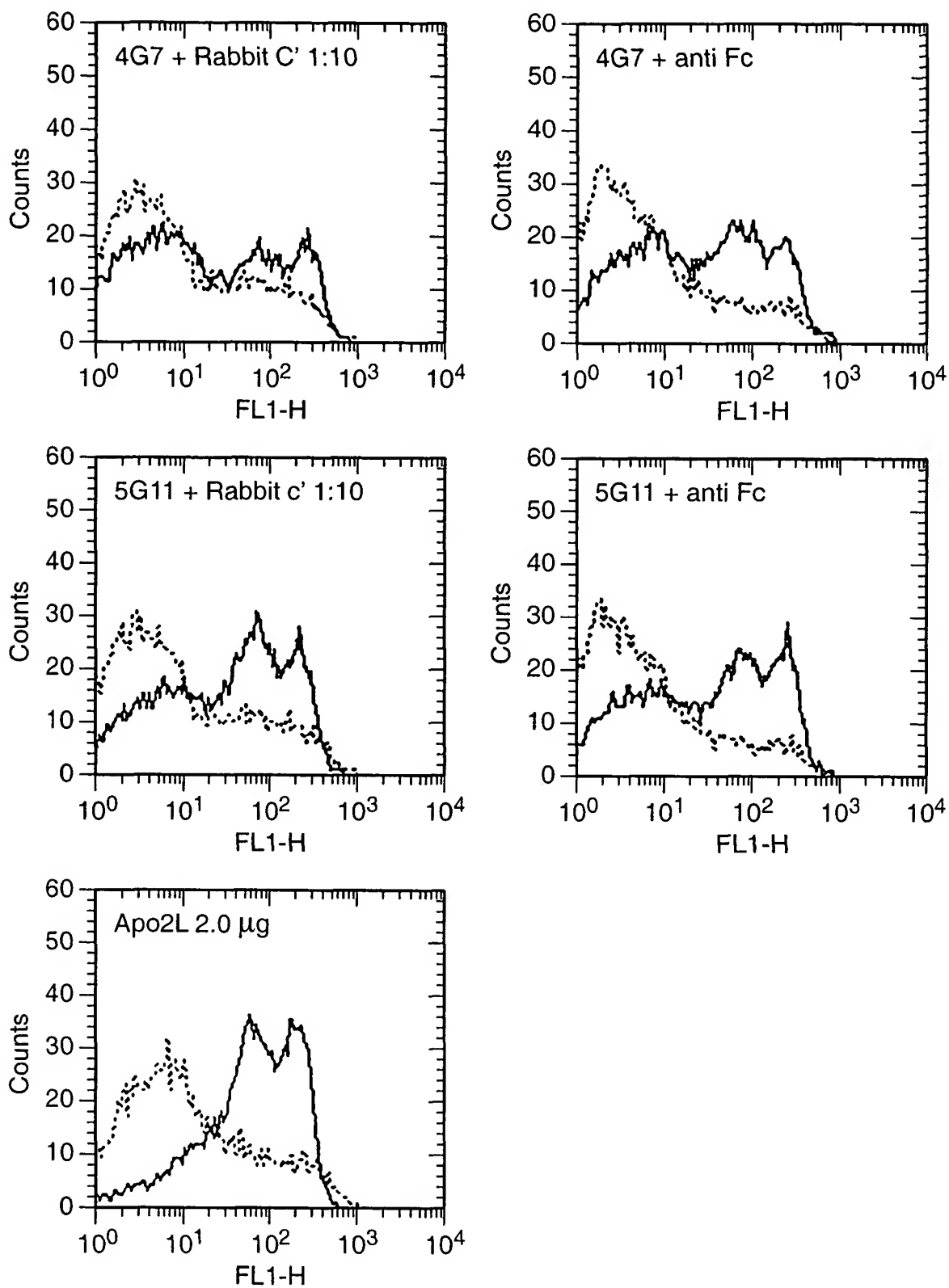


FIG._8B

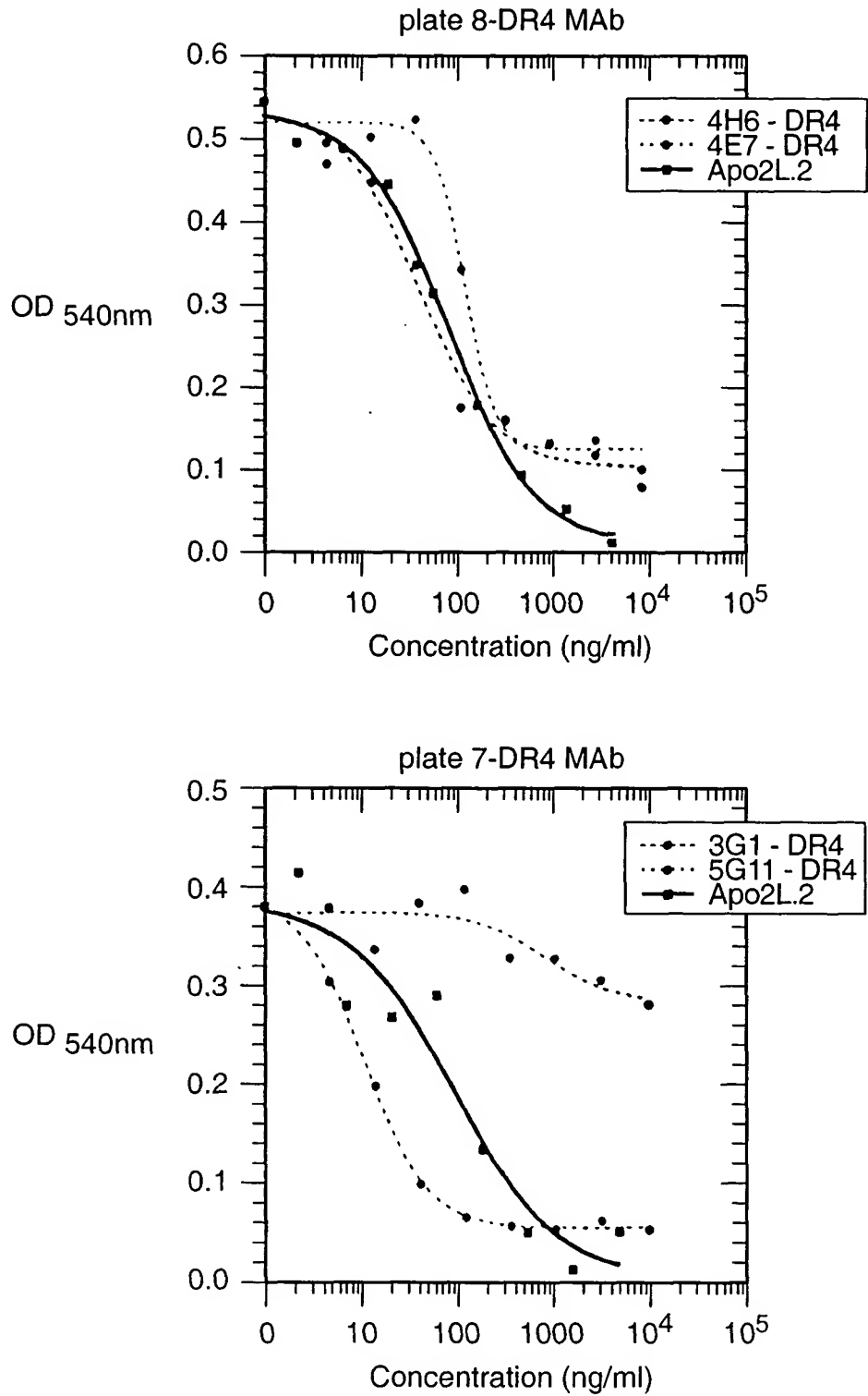


FIG. 9A

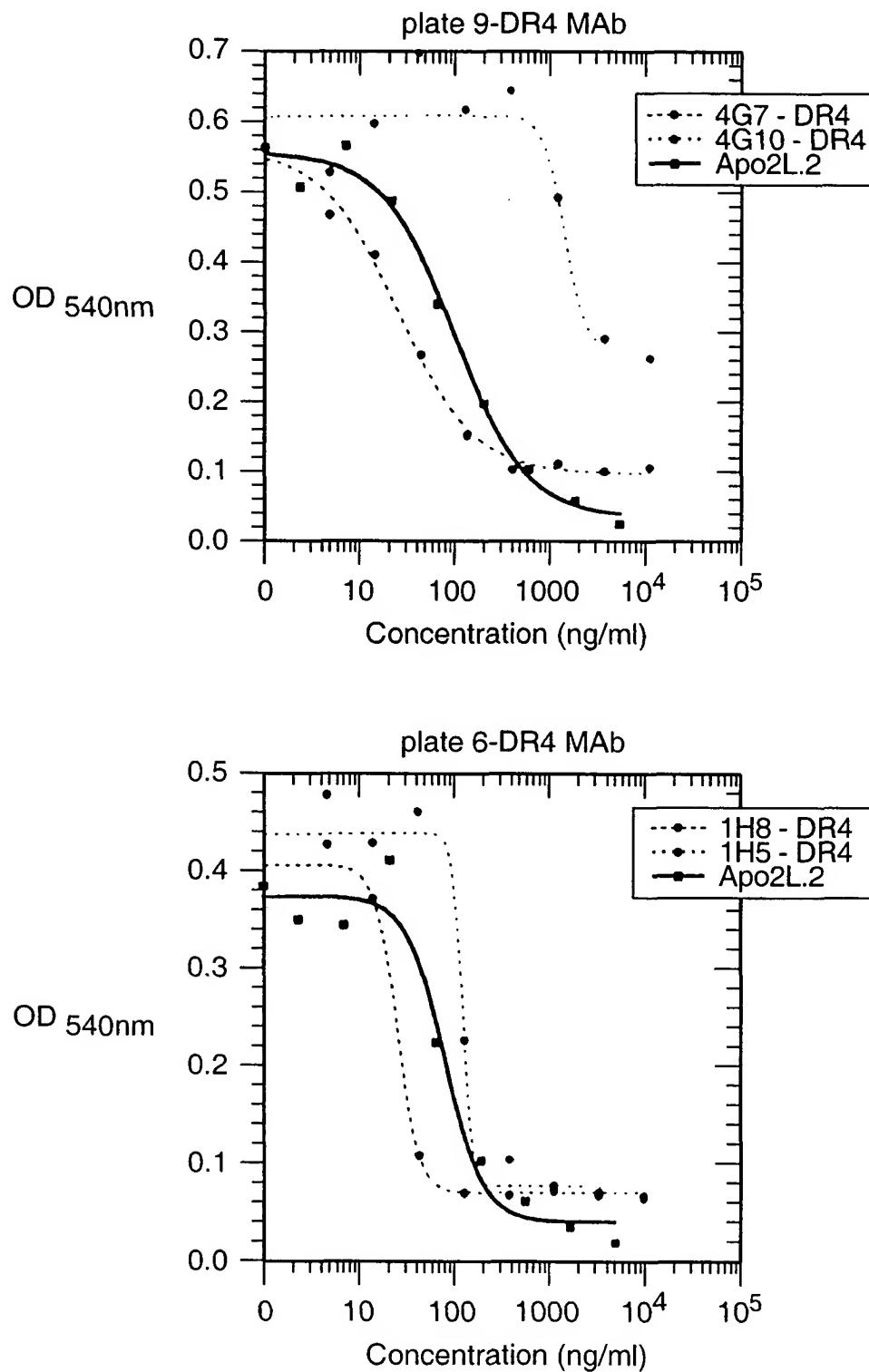
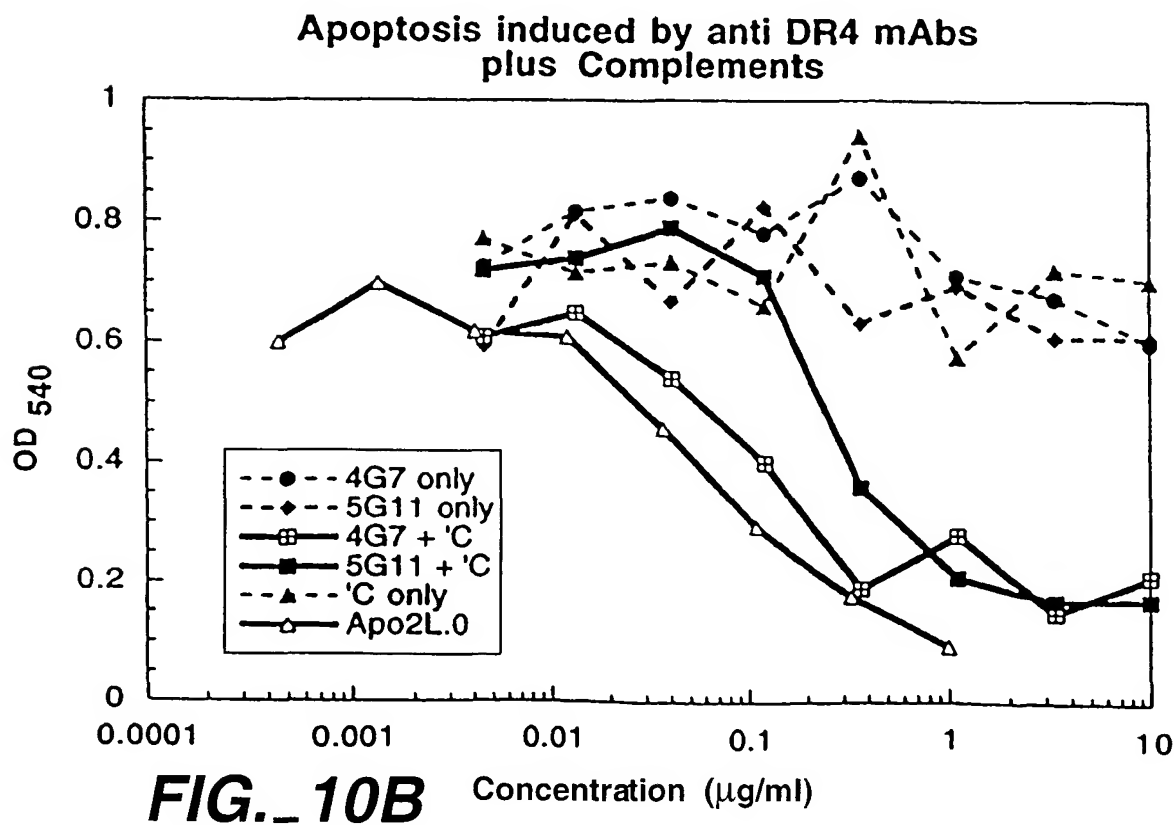
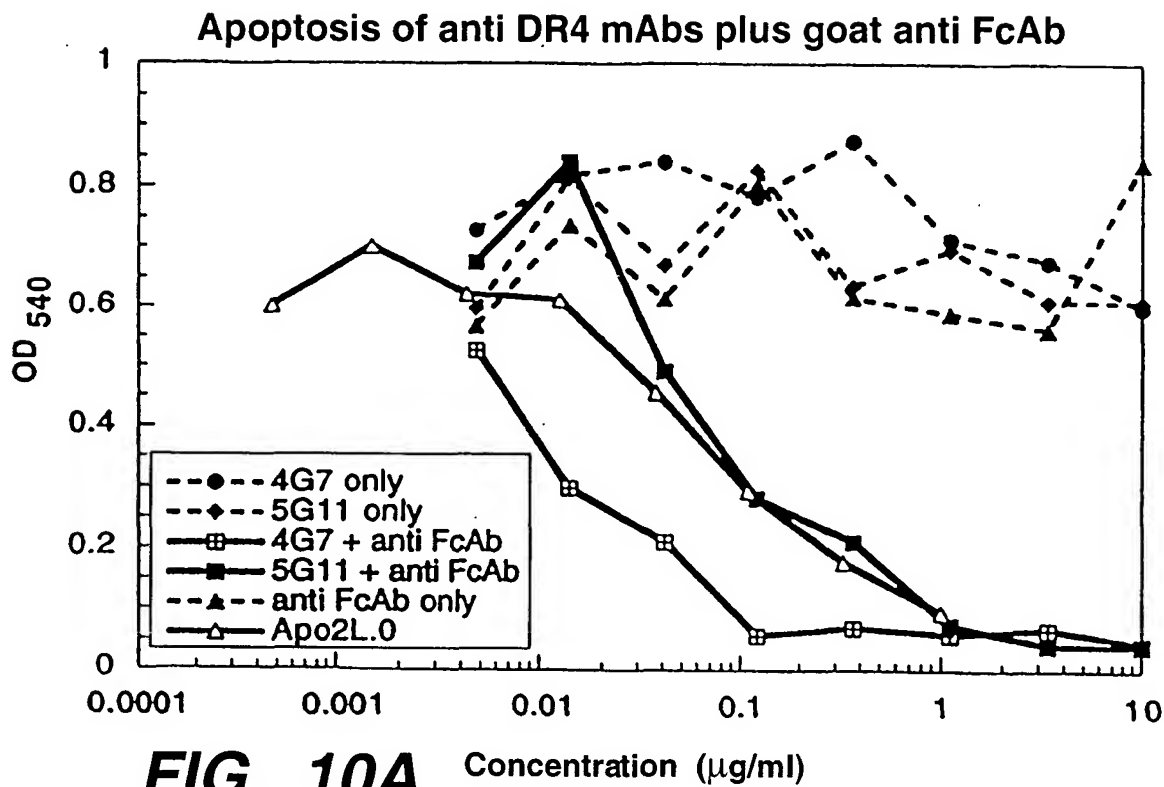
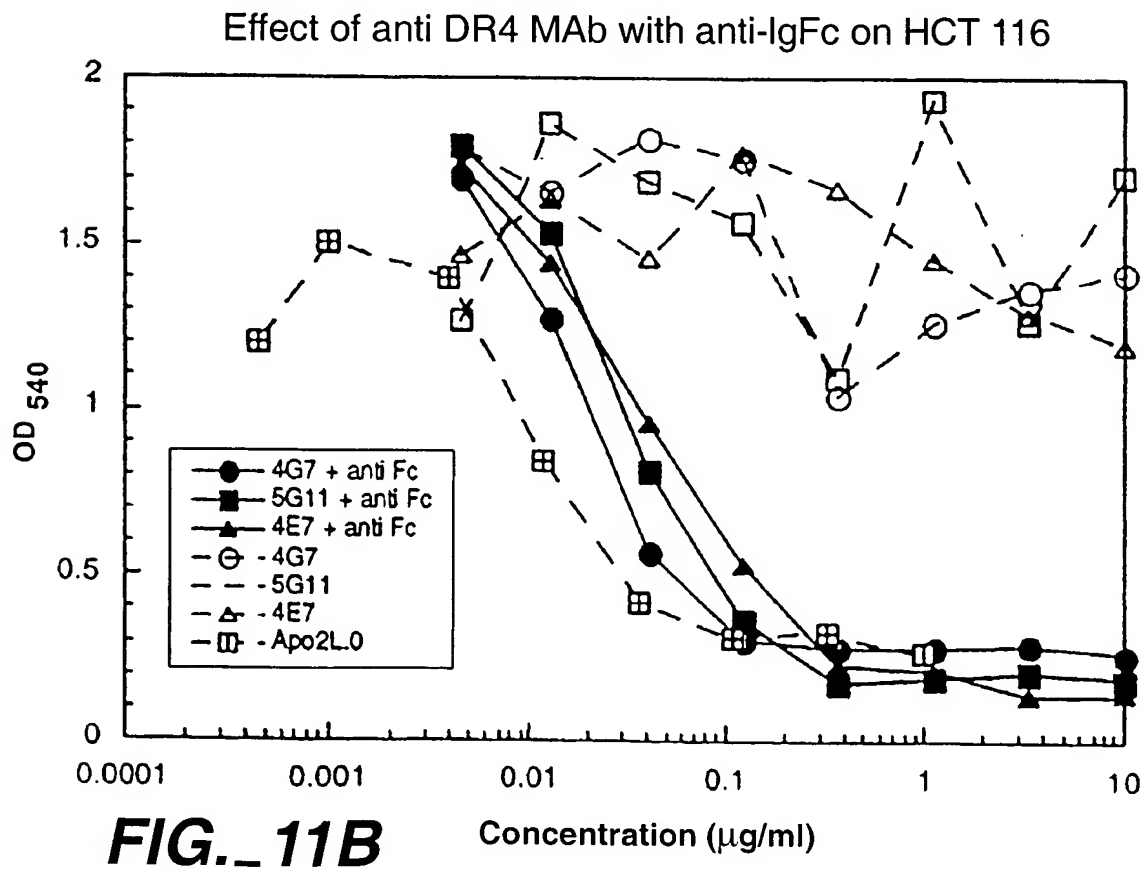
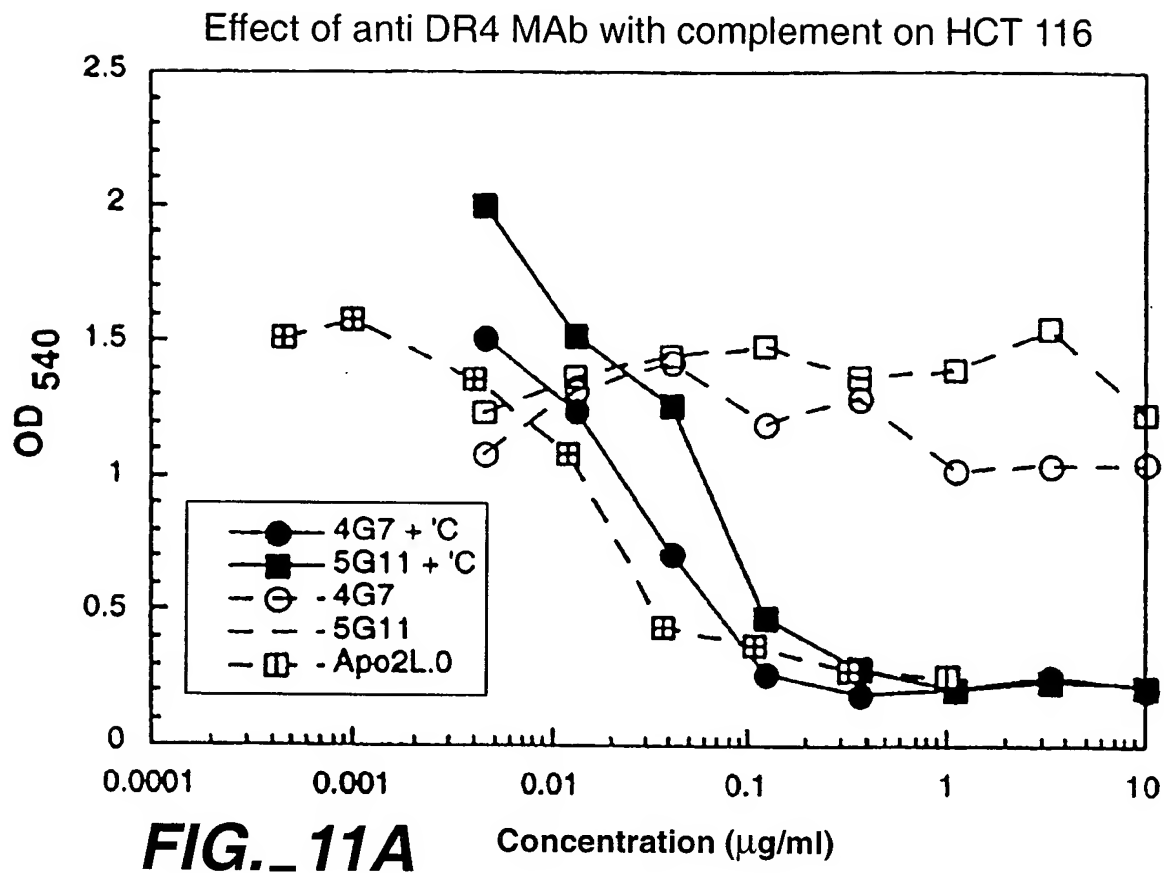


FIG._9B





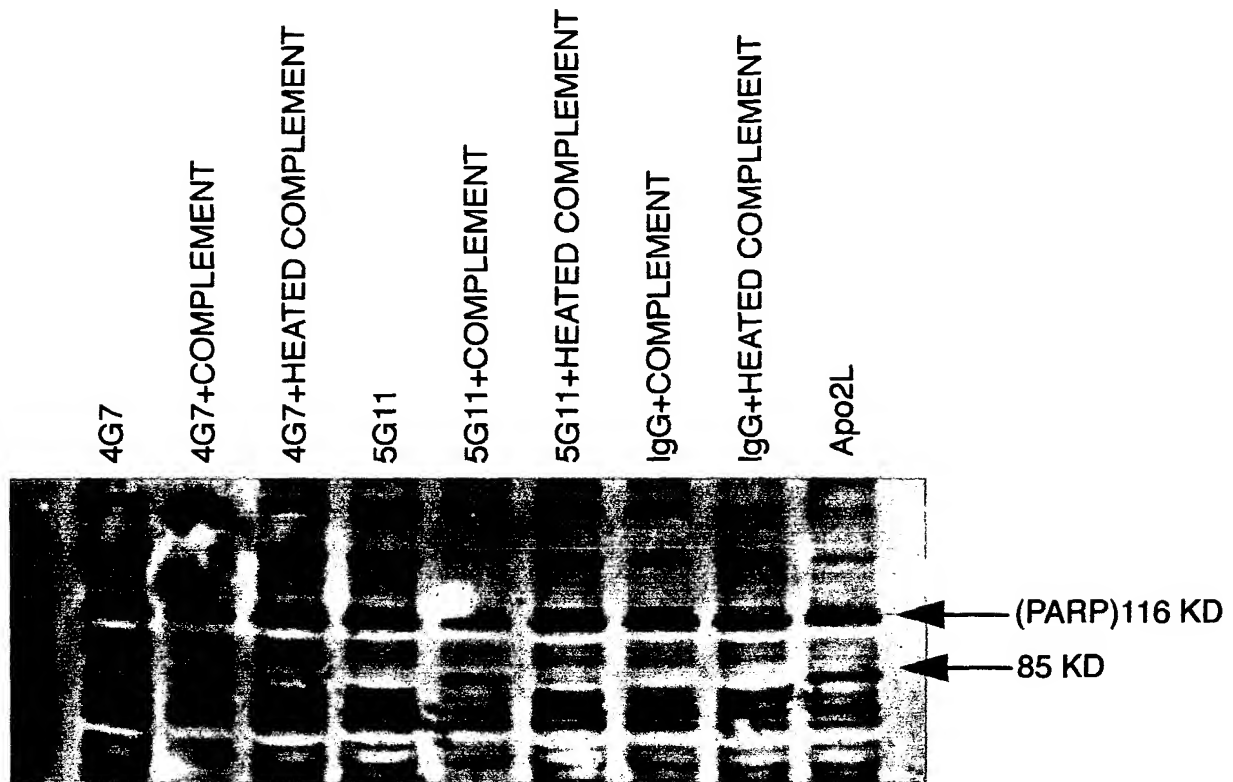


FIG. 12

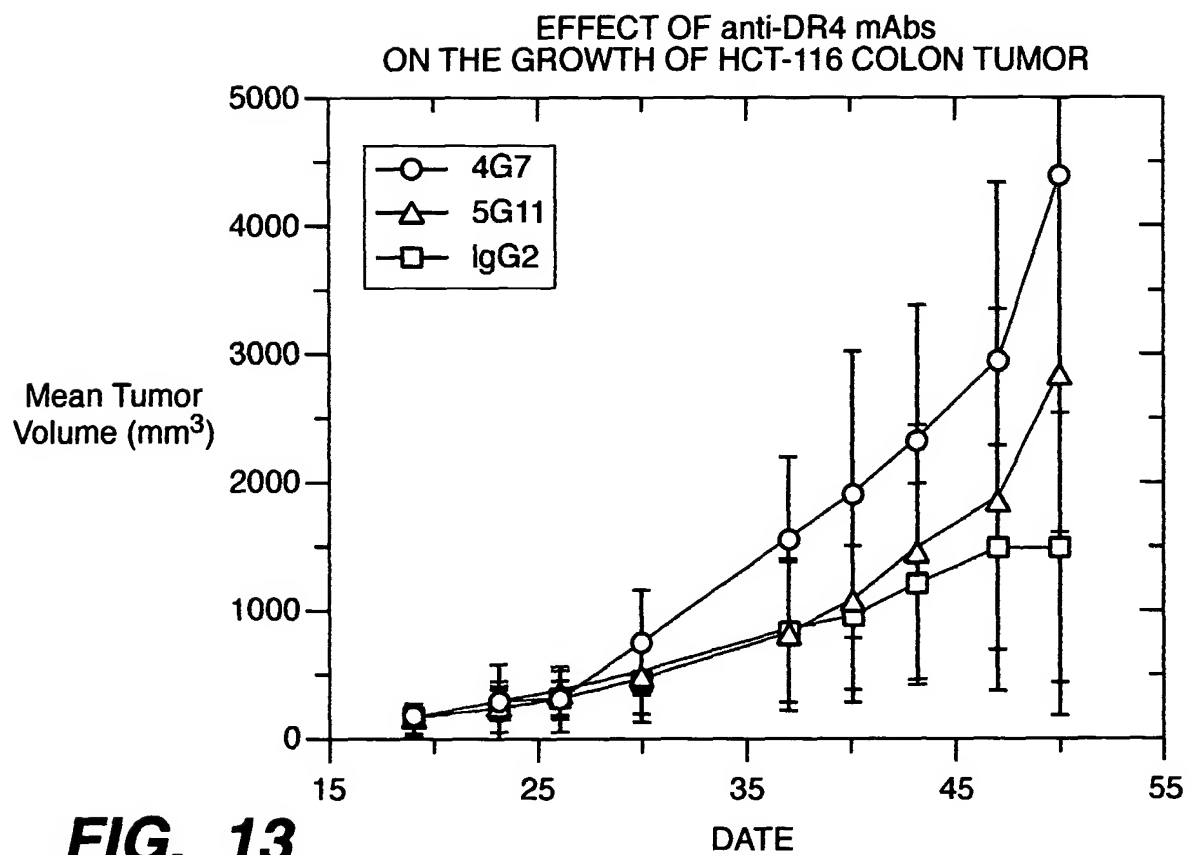


FIG. 13

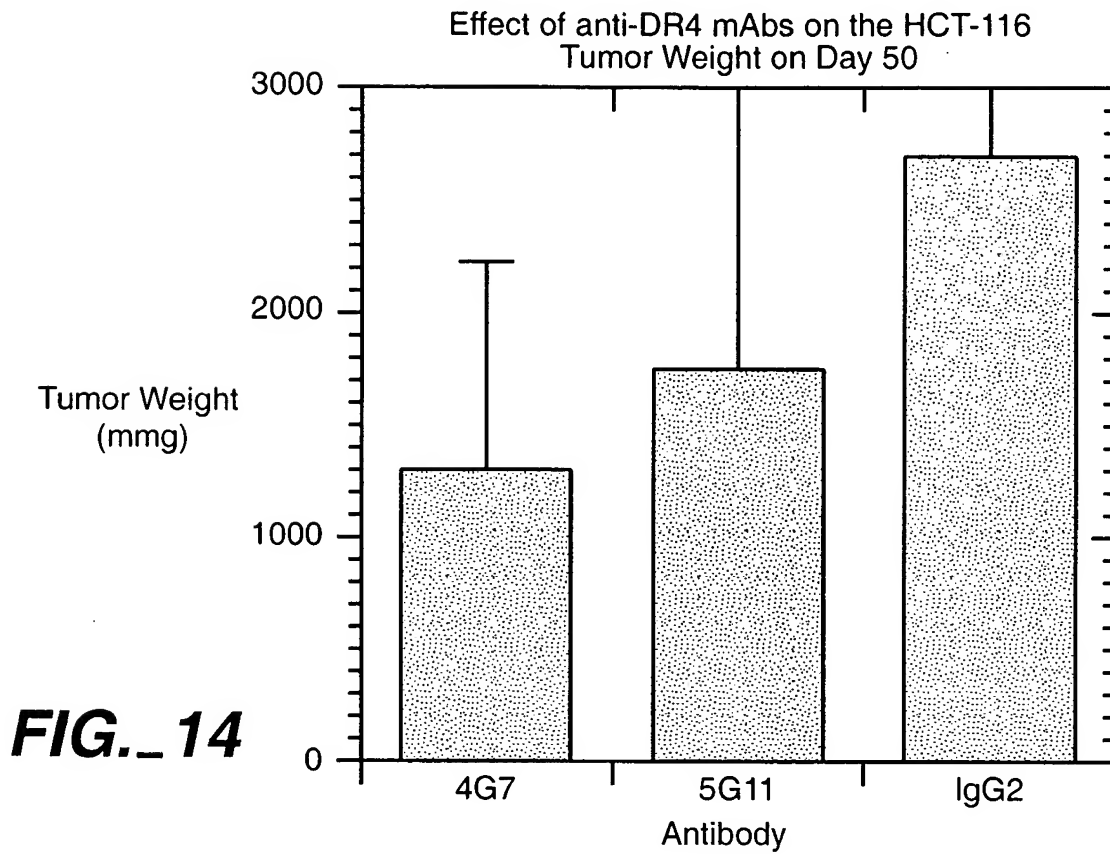


FIG._14

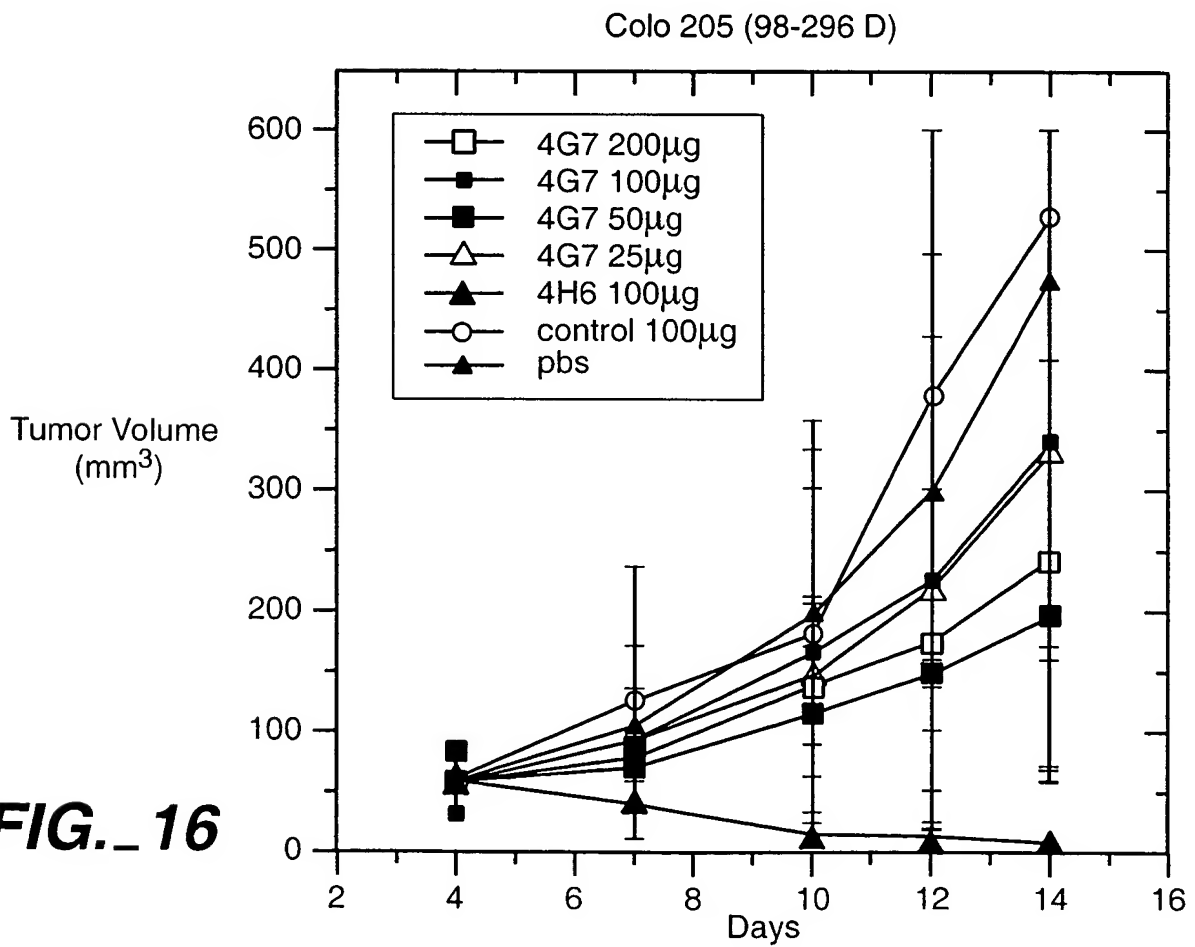


FIG._16



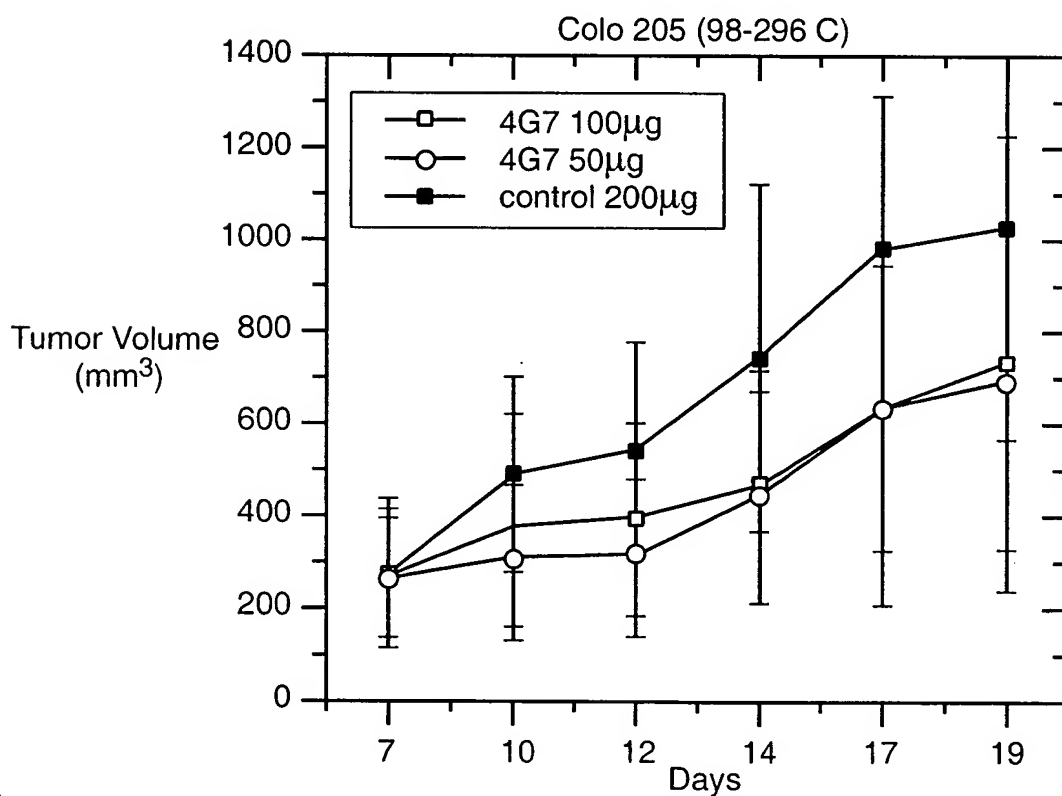
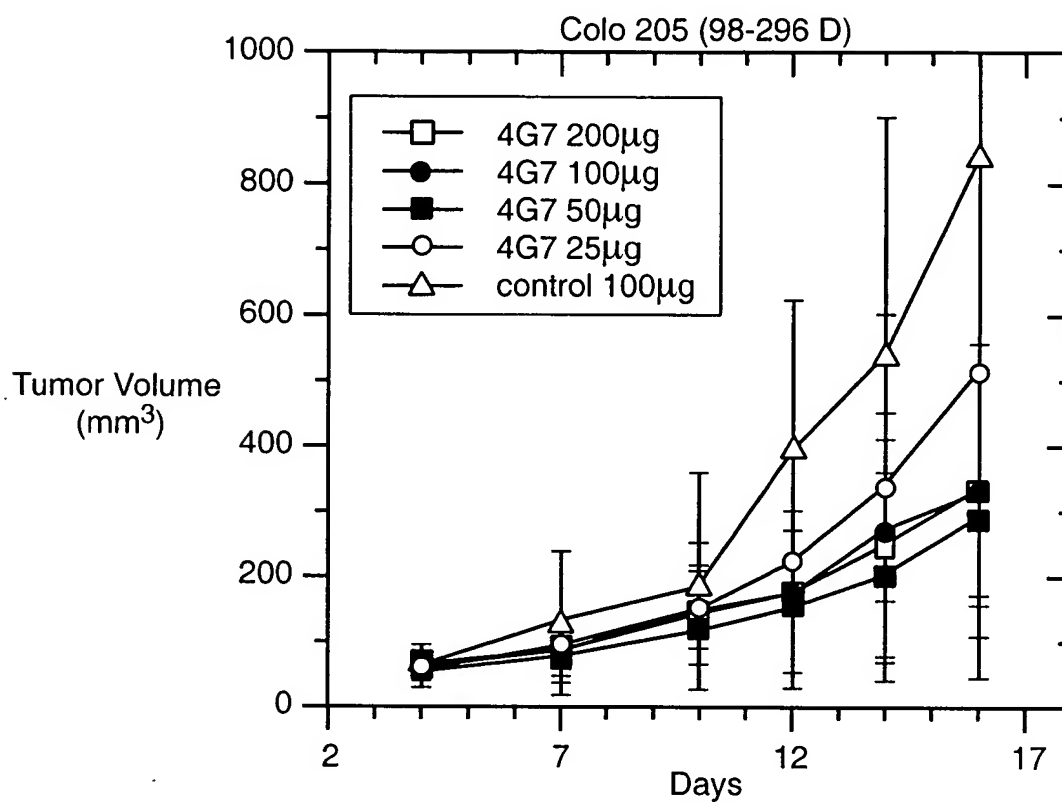


FIG. 15



GENERAL CHARACTERISTICS OF ANTI-DR4 mAbs

Isotype	Kd-1 (pm)	Apop w / o L	Apop + &Fc	Apop + C'	Block	DR4	Cross Reactivity DR5	DCR1	DCR2
1H5.24.9			-	-	ND	+++	-	-	-
1H8.17.5			+	ND	ND	+++	-	-	-
3G1.17.2			-	ND	-	+++	-	-	-
4E7.24.3	2	+ / -	+	-	-	+++	+	-	+ / -
4G7.18.8		+ / -	+	+	-	+++	-	-	-
4H6.17.8	5	+ / -	+	-	+	+++	+	-	-
4G10.20.6			+	ND	-	+++	+	-	-
5G11.17.1	22		+	+	ND	+++	++	-	-

All these mAbs recognize DR4 on 9D cells and immune precipitate DR4-IgG.
w / o L: The apoptotic ability of mAbs by themselves was detected on 9D cells, skmes cells, HCT116 and colo 205
+ &FC: The apoptotic ability of mAbs was determined in combination with goat anti-mouse IgG FC.
+ C': The apoptotic ability of mAbs was determined in the presence of rabbit complement
Degrees of binding (+) to DR5 by Mabs 4E7 and 4H6 at 10 µg / ml are 15% of the binding of DR4.

FIG._17